

Carotid artery stenting without cerebral protection

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Abstract

Carotid angioplasty and stenting is increasingly used as an attractive alternative to carotid endarterectomy (CEA) for treatment of symptomatic and asymptomatic carotid artery disease. Results from observational, non-randomised studies describe excellent technical success and periprocedural complication rates similar to those of CEA. Technical success, patency and improved complication rates are mainly the result of substantial technical improvements, an improved associated learning curve, and the improved periprocedural anti-coagulation regimens.

Currently, controversies exist as to whether carotid angioplasty with stenting should be carried out with or without obligatory use of cerebral protection. In experienced hands, the use of protection devices can decrease complication rates. However, protection systems increase catheter time and technical complexity. Reviewing the literature, the combined stroke and death rate in protected carotid angioplasty with stenting is 2.0% compared with 3.2% in unprotected carotid angioplasty with stenting, which does not strongly support the use of protection devices. Additionally, scientific evidence for the mandatory use of protection devices is lacking. Until the results of trials comparing CEA and carotid angioplasty with stenting are available, carotid artery stenting is indicated only in selected patients in an interdisciplinary approach and at high-volume centres, to obtain maximal patient benefit.

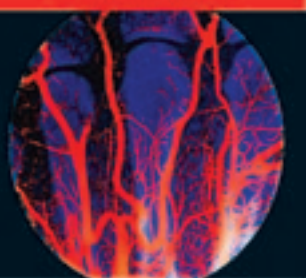
Percutaneous carotid angioplasty with stenting

During the early 1990s, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) in symptomatic patients and the Asymptomatic Carotid Atherosclerosis Study (ACAS) trial in asymptomatic patients established carotid endarterectomy (CEA) as the standard of care in patients with high-grade carotid artery stenosis.^{1,2}

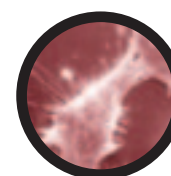
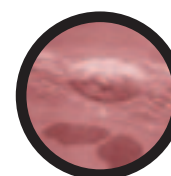
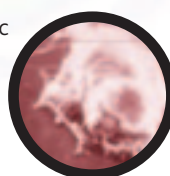
Percutaneous carotid angioplasty with stenting has the advantage of being less invasive (and thus less traumatic) but usable in patients considered to be at high surgical risk, and may therefore offer an attractive therapeutic alternative to CEA in selected patients.

Observational evidence is increasing rapidly to support the widespread use of carotid angioplasty with stenting. Results from non-randomised studies describe good technical success, and periprocedural complication rates and long-term benefits similar to those of CEA.³⁻⁵ An updated worldwide survey including more than 12,000 procedures carried out at 36 medical centres reported a technical success rate of carotid angioplasty with stenting close to 99%, a complication rate for stroke and death of <5%, and a restenosis rate of 2.4% at 3 years, respectively.⁶ However, the quality of data collection at each of these centres is difficult to ascertain and this type of survey information is subject to the bias of those reporting the information, almost certainly leading to an under-reporting of complications.

Sufficient data from randomised clinical trials comparing carotid angioplasty with stenting and CEA are still not available. The Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) was the first prospective, multicentre, randomised trial comparing carotid endovascular intervention with CEA. The interventions were carried out by operators in the learning curve, without protection devices, with contemporary appreciation for the use of aggressive anti-platelet therapy, and using state-of-the-art technical equipment. Periprocedural complication rates were equivalent for both procedures but were



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significantly higher than those seen in the single-centre studies carried out during the period 1990–1999 and those reported in NASCET and ACAS. In CAVATAS, most of the carotid angioplasty with stenting patients were treated by angioplasty alone, and stenting was conducted in only 26% of endovascular patients.⁷

The marked improvement of carotid angioplasty with stenting in the reduction in complications and improved clinical outcome is mainly the result of three factors:

(i) *Recent substantial technical improvements* – initially, the stent devices used were mainly adapted from coronary or peripheral vascular applications. Today, dedicated carotid stenting equipment with low-profile stent delivery systems, with a variety of different self-expandable stent designs, better access sheaths and specially designed wires and low profile balloons, are available.

(ii) *Increased operator experience* – as with any interventional procedure, outcomes are influenced by operator expertise and experience. The learning curve for active interventionalists beginning carotid angioplasty with stenting is very steep.

(iii) *The improved periprocedural anti-coagulation regimens* – using combined platelet inhibitors, such as acetylsalicylic acid and clopidogrel, low-molecular weight heparin before, and full heparinisation during the procedure.

Evaluation of carotid cerebral protection devices

Currently, the dominant point of discussion centres on carotid cerebral protection devices, with controversy existing as to whether carotid angioplasty with stenting should be carried out with or without cerebral protection.

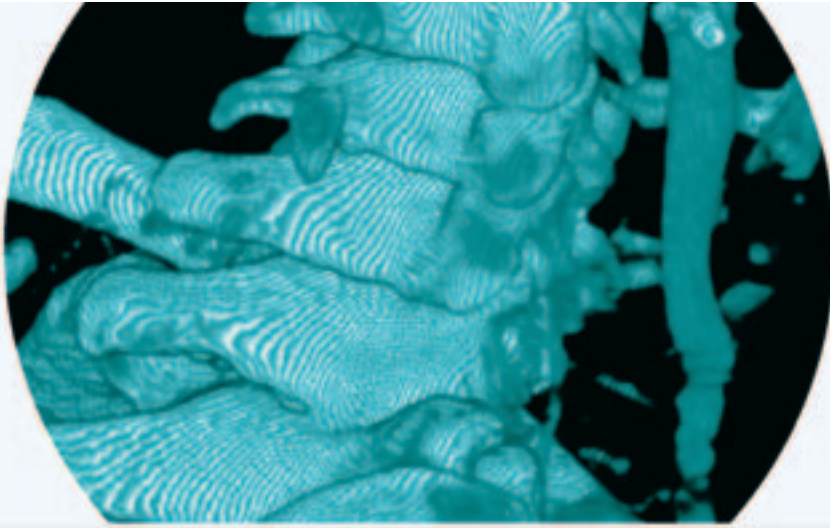
At first glance, it seems reasonable to apply protection systems to catch particles, by means of occlusive balloon systems or filtration baskets in the internal

carotid artery, before they reach the cerebral circulation, thereby minimising the risk of associated embolic neurological complications. The beneficial use of such devices seems to be supported by an increasing number of publications reporting reduced neurological complications. Theron *et al.* were the first to promote use of a distal protection device made of a triple co-axial catheter, which enabled carotid angioplasty with temporary internal carotid artery (ICA) occlusion, aspiration of debris, and flushing into the external carotid artery.⁸ Henry *et al.* further improved this technique with a commercially available low-profile occlusion balloon system.⁹ Parodi *et al.* focused on proximal embolic protection by temporarily reversing flow in the ICA,¹⁰ a technique that needs an 11 French femoral access. Recently, Cremonesi *et al.* reported their single-centre experience with protected carotid angioplasty with stenting in 442 patients with an overall complication rate of 3.4%, and a 30-day ipsilateral stroke/death rate of 1.1%, concluding that protective devices are effective in preventing distal embolisation.¹¹

However, the published data come from uncontrolled trials with variable patient selection and are collected retrospectively. Alternatively, the collection of data is not otherwise unbiased, for example, in industry-sponsored trials or where the investigators are affiliated to the companies developing or distributing the devices.

Kastrup *et al.* systematically reviewed single-centre carotid angioplasty with stenting studies from 1996 to 2003.¹² The combined stroke and death rate within 30 days was 1.8% in carotid angioplasty with stenting with protection compared with 5.5% in carotid angioplasty with stenting without protection.

The authors concluded that protection devices appear to reduce thromboembolic complications during carotid angioplasty with stenting.¹² However, patients were treated under very heterogeneous conditions. When concentrating on the studies appearing since 2002,



when patients were treated under more comparable conditions incorporating technical and anti-coagulation progress, the combined stroke and death rate within 30 days in protected carotid angioplasty with stenting was 2.0% compared with 3.2% in unprotected carotid angioplasty with stenting. This does not, in our view, justify a strong recommendation of the use of protection devices.¹¹⁻²⁰

As a result of this low complication rate without the use of protection devices we, like many other neurointerventionalists, continue to successfully carry out carotid artery stenting (CAS) without the use of cerebral protection in our everyday clinical practice (Figures 1 and 2). In centres in which experience with unprotected carotid angioplasty with stenting has been gathered, scepticism surrounds the assumed self-

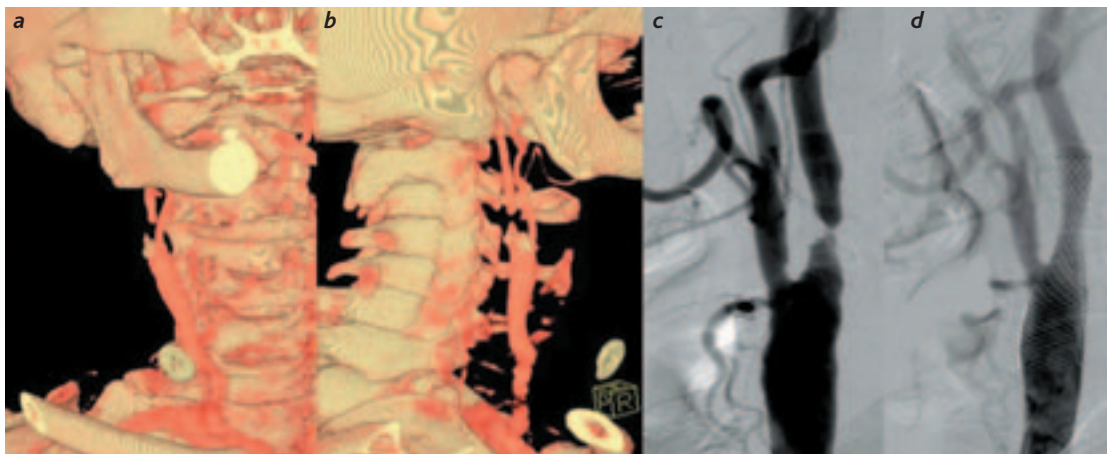


Figure 1. A 71-year-old man presenting with a transient left sided hemiparesis. CT angiography (maximum intensity projection (MIP) reconstruction) shows severe calcified stenosis of the origin of the right internal carotid artery (a, b). Digital subtraction angiogram after right carotid artery injection before (c) and after (d) successful stent implantation without cerebral protection.

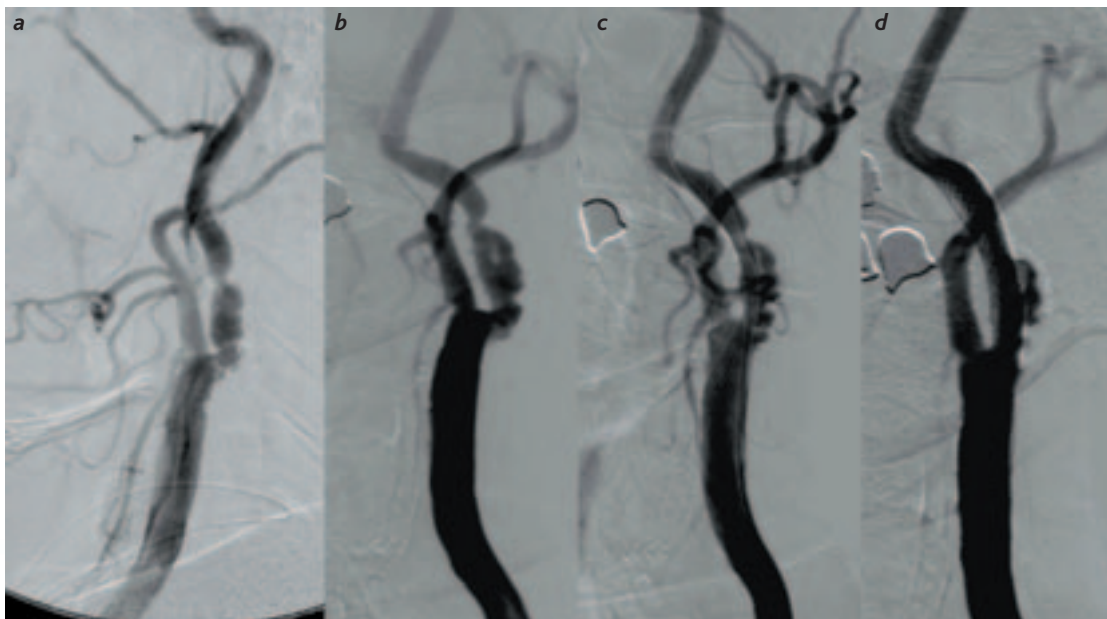


Figure 2. A 62-year-old man presenting with a history of amaurosis fugax. Digital subtraction angiogram shows severe ulcerated stenosis of the internal carotid artery (a, b). Further images shown are after unprotected stent deployment before dilation (c) and the final result after dilation of the stent (d).

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evident improvement on implementation of protection devices. This is based not only on the low complication rate without them, but also on the technical complications related to their use, which are apparently poorly reported up to now.

Disadvantages of cerebral protection systems

Cerebral protection systems have themselves some inherent disadvantages, namely an increase in both catheter time and technical complexity, both of which might be associated with an increased complication rate. The advantage of filter systems is that they provide continuous perfusion to the brain.

The disadvantages for some systems include a larger diameter than distal balloon occlusions, difficulties in tracking more angulated bifurcations and tortuous vessels, and the theoretical issue of missing very small particles. Balloon devices comprise the second group of embolic protection devices. The principal disadvantage of these is that 5–10% of patients do not tolerate carotid occlusion.⁹ Rarely, significant dissection of the internal carotid artery occurs. Another disadvantage is that angiography during the procedure is not possible.

The primary passage of the stenosis must always be an unprotected manoeuvre. Passing more instrumentation across friable plaque can itself lead to complications,¹¹ such as cerebral embolism, vasospasm or, rarely, dissection. Primary stenting, i.e. stent implantation before the first balloon inflation, may also help to prevent distal embolisation by fixation of the debris to the vessel wall. However, clinically relevant embolisation may still occur. As a result of the larger diameter of the protection devices, pre-dilatation of the stenosis is often necessary before the protection device may be placed. Transcranial Doppler imaging studies report pre-dilatation as the most dangerous step of carotid angioplasty with stenting.¹⁸ In the study of Cremonesi *et al.*¹¹ pre-dilatation was necessary in 37% of patients compared with only 2% of patients for unprotected

carotid angioplasty with stenting.^{11,19} After stent placement and post-dilatation, removal of protection devices may cause additional microembolisation.²¹ Thus, from a procedural point of view, protection devices may reduce, but do certainly not eliminate, plaque embolisation.

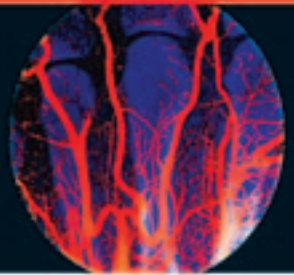
A requirement for data from comparative trials

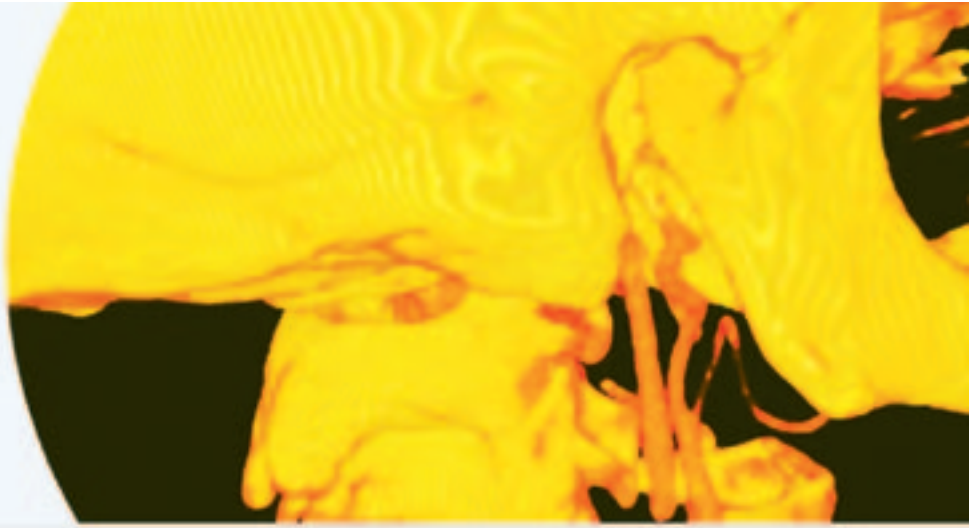
In addition to the factors discussed above, quality of evidence for the use of protection devices is still lacking.²⁰ As a result of the low complication rate of carotid angioplasty, even without cerebral embolic protection devices, large randomised trials are necessary to prove the clinical efficacy of these devices. Thus, all efforts should concentrate on finishing the ongoing trials comparing CEA and carotid angioplasty with stenting[†], such as SPACE (Germany), CAVATAS (United Kingdom), EVA-3S (France) and CREST (United States). It is anticipated that these trials will publish definitive results within the next 1–3 years and help guide the referral of patients for carotid angioplasty with stenting and CEA in the future. Until these results are available, no scientific evidence is available to support the use of carotid angioplasty with stenting over CEA in appropriate patients or the use of carotid angioplasty with stenting in asymptomatic patients.

Indications for carotid angioplasty with stenting

In our opinion, the only generally accepted indication for carotid angioplasty with stenting outside of clinical trials is patients with medical contraindications to CEA, post-radiation carotid stenosis, restenosis of a previous CEA, high cervical anatomically inaccessible lesions, or contralateral carotid occlusions.

Importantly, carotid angioplasty should be carried out as an interdisciplinary approach in centres with a sufficient case-load where an experienced team of interventional neuroradiologists and neurologists closely collaborate to obtain maximal patient benefit.





Trials comparing CEA and carotid angioplasty with stenting:
SPACE (Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy)
CAVATAS (Carotid and Vertebral Artery Transluminal Angioplasty Study)
EVA-3S (Endarterectomy Versus Angioplasty in Patients With Symptomatic Severe Carotid Stenosis)
CREST (Carotid Revascularization Endarterectomy versus Stent Trial)

Key Learning

- Carotid angioplasty with stenting is increasingly used as a less invasive alternative to carotid endarterectomy in patients with carotid artery disease
- Improvements in technology, anti-coagulation regimens and operator experience have reduced complication rates and improved the clinical outcome from carotid angioplasty with stenting
- The use of cerebral protection devices during carotid angioplasty with stenting is controversial and scientific evidence for the obligatory use is still lacking
- Use of cerebral protection devices has disadvantages including:
 - increased catheter time
 - increased technical complexity
 - in some cases pre-dilatation of stenosis with the risk of plaque embolisation
- Carotid angioplasty with stenting can be successfully carried out without cerebral protection in routine clinical practice
- Ongoing clinical trials will provide better evidence on the clinical efficacy of cerebral protection devices

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